VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

Bexxar (tositumomab-I131)

Effective Date: 10/22/13
Date Developed: 9/3/13 by Albert Reeves MD
Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20, 8/3/21, 2/1/22, 1/31/23, 2/13/24, Archived 1/2/25

BEXXAR DISCONTINUED FEBRUARY 20, 2014- use of generic forms will be assessed on a case-by-case basis.

Tositumomab-I131 is an antineoplastic monoclonal antibody that is linked with radioactive iodine I-131 designed to destroy only certain cells in the body.

Preauthorization Criteria: Treatment of relapsed or refractory CD20 positive, low-grade, follicular, or transformed non-Hodgkin's lymphoma (NHL), with progression during or after rituximab treatment

Administration: I.V.

Note: BEXXAR therapeutic regimen is only indicated for a single course of treatment and is not indicated for a first-line treatment. Refer to manufacturer's labeling for additional details

Dosage:

I.V.: Dosing consists of four components administered in 2 steps*. Refer to manufacturer's labeling for additional details*. Indicated for a single treatment course. Thyroid protective agents (SSKI, Lugol's solution or potassium iodide) should be administered beginning at least 24 hours prior to step 1. Premedicate with acetaminophen 650 mg and diphenhydramine 50 mg orally 30 minutes prior to step 1 and step 2.

Step 1: Dosimetric step (Day 0):

Tositumomab 450 mg administered over 60 minutes

Iodine I 131 tositumomab (containing I-131 5 mCi and tositumomab 35 mg) administered over 20 minutes

Note: Whole body dosimetry and biodistribution should be determined on Day 0; days 2, 3, or 4; and day 6 or 7 prior to administration of Step 2. If biodistribution is not acceptable, do not administer the therapeutic step. On day 6 or 7, calculate the patient specific activity of iodine I 131 tositumomab to deliver 75 cGy total body dose (TBD) or 65 cGy TBD (in mCi).

Step 2: Therapeutic step (one dose administered 7-14 days after step 1):

Tositumomab 450 mg administered over 60 minutes followed by Iodine I 131 tositumomab (containing I-131 5 mCi and tositumomab 35 mg) over 20 minutes

NOTE:

Platelets ≥150,000/mm^3: Iodine I 131 calculated to deliver 75 cGy total body irradiation and tositumomab 35 mg over 20 minutes

Platelets ≥100,000/mm^3 and <150,000/mm^3: Iodine I 131 calculated to deliver 65 cGy total body irradiation and tositumomab 35 mg over 20 minutes

Precautions:

Prior to infusion, patients should be premedicated (with acetaminophen and an antihistamine) and a thyroid-protective agent should be started. Reduce the rate of tositumomab or iodine 131 tositumomab infusion by 50% for mild-to-moderate infusion-related toxicities; interrupt for severe infusion reaction (once severe infusion reaction has resolved, infusion may be restarted at half the previous rate). Discontinue for serious allergic reaction.
Check product information for use in specific populations

Major adverse reactions:

>10%:

Central nervous system: Fever (37%), pain (19%), chills (18%), headache (16%)

Dermatologic: Rash (17%)

Endocrine & metabolic: Hypothyroidism (7% to 19%)

Gastrointestinal: Nausea (36%), abdominal pain (15%), vomiting (15%), anorexia (14%), diarrhea (12%)

Hematologic: Myelosuppression (grades 3/4: 71%; nadir: 4-7 weeks; duration: ~30 days), neutropenia (grades 3/4: 63%; median duration: 31 days; grade 4: 25%), thrombocytopenia (grades 3/4: 53%; median duration: 32 days; grade 4: 21%), lymphocytopenia (recovery: ~12 weeks after treatment), anemia (grades 3/4: 29%; median duration: 23 days; grade 4: 5%), secondary leukemia/myelodysplastic syndrome (overall: 3% to 10%; 2-year follow-up: 2% to 5%; 5-year follow-up: 6% to 15%), hemorrhage (12%)

Neuromuscular & skeletal: Weakness (46%), myalgia (13%)

Respiratory: Cough (21%), pharyngitis (12%), dyspnea (11%)

Miscellaneous: Infusion-related reactions (29%, occurred within 14 days of infusion, included bronchospasm, chills, dyspnea, fever, hypotension, nausea, rigors, diaphoresis); infection (21% to 45%, serious: 9%);g HAMA-positive seroconversion (10% to 11%)

BOXED WARNINGS:

Serious Allergic Reactions (Including Anaphylaxis): Serious, including fatal, allergic reactions have occurred during or following administration of the BEXXAR therapeutic regimen. Have medications for the treatment of allergic reactions available for immediate use.

Prolonged and Severe Cytopenias: The BEXXAR therapeutic regimen resulted in severe and prolonged thrombocytopenia and neutropenia in more than 70% of the patients in clinical studies. The BEXXAR therapeutic regimen should not be administered to patients with greater than 25% lymphoma marrow involvement, platelet count less than 100,000 cells/mm3 or neutrophil count less than 1,500 cells/mm3.

Radiation Exposure: The BEXXAR therapeutic regimen may be administered only under the supervision of physicians who are certified under or participating in the BEXXAR therapeutic regimen certification program and who are authorized under the Radioactive Materials License at their clinical site.

Dosage Forms:

Tositumomab 225 mg solution (14 mg per mL), single use vial

Tositumomab 35 mg solution (14 mg per mL), single use vial

Iodine I 131 tositumomab solution containing 12-18 mCi Iodine-131 per vial (not less than 0.61 mCi per mL at calibration) and 2.0-6.1 mg tositumomab per vial (not less than 0.1 mg per mL), single use vial

Iodine I 131 tositumomab solution containing 112-168 mCi Iodine-131 per vial (not less than 5.6 mCi per mL at calibration) and 22-61 mg tositumomab per vial (not less than 1.1 mg per mL), single use vial

Contraindications

There are no contraindications listed in the manufacturer's labeling.

References:

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2. Kaminski MS, Radford JA, Gregory S, et al, "Re-Treatment With I-131 Tositumomab in Patients With Non-Hodgkin's Lymphoma Who Had Previously Responded to I-131 Tositumomab," *J Clin Oncol*, 2005, 23(31):7985-93. [PubMed 16204016]
3. Kaminski MS, Tuck M, Estes J, et al, "131I-Tositumomab Therapy as Initial Treatment for Follicular Lymphoma," *N Engl J Med*, 2005, 352(5):441-9. [PubMed 15689582]

4. Kaminski MS, Zelenetz AD, Press OW, et al, “Pivotal Study of Iodine I 131 Tositumomab for Chemotherapy-Refractory Low-Grade or Transformed Low-Grade B-Cell Non-Hodgkin's Lymphomas,” *J Clin Oncol*, 2001, 19(19):3918-28. [PubMed 11579112]
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6. Press OW, Eary JF, Appelbaum FR, et al, “Phase II Trial of 131I-B1 (Anti-CD20) Antibody Therapy With Autologous Stem Cell Transplantation for Relapsed B Cell Lymphomas,” *Lancet*, 1995, 346(8971):336-40.
7. Press OW, Unger JM, Braziel RM, et al, “Phase II Trial of CHOP Chemotherapy Followed by Tositumomab/Iodine I-131 Tositumomab for Previously Untreated Follicular Non-Hodgkin's Lymphoma: Five-Year Follow-up of Southwest Oncology Group Protocol S9911,” *J Clin Oncol*, 2006, 24(25):4143-9. [PubMed 16896003]
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9. FDA Prescribing Information: https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/125011s0126lbl.pdf
10. https://journals.lww.com/oncology-times/blog/onlinefirst/lists/posts/post.aspx?List=45ae9d5c-1d65-4f9e-855c-744e5e66fe80&ID=800&Web=4df07b86-f4aa-4c34-8e9a-12c5b627c78e

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Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
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2/18/25	Yes	Howard Taekman, MD; Robert Sterling, MD	Added "BEXXAR DISCONTINUED FEBRUARY 20, 2014- use of generic forms will be assessed on a case-by-case basis." Removed pharmacologic category section. Added Tositumomab-I131 definition and modified the dosage section